UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,448	03/26/2001	H. Craig Dees	PHO-120	2388

7590 09/23/2003

Edward D. Manzo, Esq.
COOK, ALEX, MCFARRON, MANZO
CUMMINGS & MEHLER, LTD.
200 West Adams St., Suite 2850
Chicago, IL 60606

EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/23/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/817,448	DEES ET AL.	
	Examin r	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears n the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *41-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40 and 46-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-50* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 4/28/03 in Paper No. 10 is acknowledged and has been entered. Claims 1-40 and 46-50 have been amended. Claims 41-45 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Currently, claims 1-50 are pending and claims 1-40 and 46-50 are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 112

2. In light of Applicant's amendment, the rejection of claims 1-10, 12-15, 29-40, and 46-50 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.

3. In light of Applicant's argument, the rejection of claims 6, 7, 34, and 35 under 35 U.S.C. 112, first paragraph, is hereby, withdrawn.

4. In light of Applicant's submission of a terminal disclaimer, the provisional obviousness-type double patenting rejection of claims 1-40 and 46-50 is hereby, withdrawn.

5. In light of Applicant's argument, the rejections of claims 1-40 and 46-50 under 35 U.S.C. 102 and 103, as being anticipated by Gulliya et al. (US 5,177,073) are hereby, withdrawn.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 11 and 16-28 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is vague and indefinite in reciting, "for the treatment of indications" because it is unclear what is encompassed by the term "indications" and how it relates to the diseases.

Claim 16 provides for the use of a halogenated xanthene, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 16-28 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Regarding claim 17, the phrase "related organs" renders the claim indefinite because the claim includes elements not actually disclosed (those

encompassed by "related organs"), thereby rendering the scope of the claim unascertainable.

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 8-33, 36-40 and 46-50 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a medicament or pharmaceutical composition which functions in combination with ionizing radiation for treating diseased cancer, infected, and lipocytic tissue, does not reasonably provide enablement for treating all other diseased tissue, such as vascular and nasal tissue, involved in coronary artery disease, myocardial infarction, and allergic reaction conditions, respectively, as an example. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The claimed invention is drawn to a medicament or a pharmaceutical composition *comprising* halogenated xanthene as a primary active component, which is used in combination with ionizing radiation, for phototherapeutic treatment of human or animal tissue. Accordingly,

8. Claims 1, 3, 5, 8-12, 15-18, 20, 29, 31, 33, 36-39, 46-48, and 50 stand rejected under 35 U.S.C. 102(b) as being anticipated by Serafini et al. (Journal of Nuclear Medicine, 1975) for reasons of record.

9. Claims 1, 3, 5, 8-10, 12, 16, 18, 20, 29, 31, 33, 36-39, 46-48, and 50 stand rejected under 35 U.S.C. 102(b) as being anticipated by Neckers D. (Journal of Photochemistry and Photobiology, A: Chemistry 47: 1-29 (1989)) for reasons of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 14 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Neckers D. (Journal of Photochemistry and Photobiology, A: Chemistry 47: 1-29 (1989)) in view of Norman et al. (Invest Radiol, 26: S120-S121, 1991) for reasons of record or as follows.

Neckers has been discussed supra. Neckers differs from the instant invention in failing to teach applying ionizing radiation at specifically greater than approximately 1 keV and less than approximately 1000 MeV.

Norman et al. teach pharmaceutical compositions that comprise iodinated contrast media such as gandolinium, for treatment of diseased tissue by applying ionizing radiation wherein doses absorbed from diagnostic X-rays are enhanced. Norman et al. specifically teach that the contrast media exhibit preference to

localize at biologically sensitive diseased tumor tissues. Norman et al. also teach that dose enhancement factor (DEF) which increases linearly with the concentration of halogen, i.e. iodine, can be achieved with other conventional ways of administering the contrast media (S120, column 1 and 2). Figure 1 shows a plot of the DEF as a function of the iodine concentration in a lymphocyte medium during irradiation at 140 keV. According to Norman et al., the therapeutic ratio, the ratio of radiation dose absorbed by a diseased brain tumor tissue versus that absorbed by the surrounding normal brain tissues increases with increasing contrast medium in the diseased tissue.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to activate the halogenated xanthene or Rose Bengal, taught by Neckers with ionizing radiation at 140 keV as taught by Norman because Norman specifically taught applying ionizing radiation at 140 kEV upon gandolinium, which belongs to the same class of halogenated, i.e. iodinated, contrast medium, as the halogenated xanthenes as taught by Neckers, and the halogenated xanthenes or Rose Bengal are obvious variations of iodinated contrast media known in the art and which have been taught by Neckers as being characteristically capable of photodynamic and radiation activation.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

11. Claims 1, 3-5, 16, 18, 19, 29, 31-33, 46, 47, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Fondren et al. (Environ Entomol (1978)).

Fondren et al. enumerate six xanthene dyes and describe their relative toxicities. Specifically, Fondren et al. teach that xanthene dyes, among others include rose bengal, octabromofluorescein, erythrosin B, phloxin B, eosin Y, and tetrachlorofluorescein.

Claim Rejections - 35 USC § 103

12. Claims 2 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Serafini et al. (Journal of Nuclear Medicine, 1975) or Neckers D. (Journal of Photochemistry and Photobiology, A: Chemistry 47: 1-29 (1989)) or Fondren et al. (Environ Entomol (1978)).

Serafini et al., Neckers, and Fondren et al. have been discussed supra. Serafini et al., Neckers, and Fondren et al. differ from the instant invention in failing to disclose that halogenated xanthene is present in the concentration of 0.001% to less than 20%.

However, the concentration of halogenated xanthene in relation to the aqueous mixtures of the compound, constitute result effective variables which have been shown may be altered depending on how xanthene is used or the tissue being treated in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is

involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the concentration range recited in instant claims 2, 27, and 30 are for any particular purpose or solve any stated problem and prior art has shown that concentrations often vary according to use and purpose of the compound, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the active ingredient concentrations disclosed by the prior art by normal optimization procedures.

13. Claim 6, 7, 13, 21, 34, 35, 40, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Serafini et al. (Journal of Nuclear Medicine, 1975) or Neckers D. (Journal of Photochemistry and Photobiology, A: Chemistry 47: 1-29 (1989)) or Fondren et al. (Environ Entomol (1978)) in view of Khaw et al. (US 5,780,052).

Serafini et al., Neckers, and Fondren et al. have been discussed supra. Serafini et al., Neckers, and Fondren et al. differ from the instant invention in failing to disclose incorporating the halogenated xanthenes into specific delivery systems for enhanced targeting towards specific localized tissues. Serafini et al., Neckers, and Fondren et al. differ from the instant invention in failing to disclose that the ionizing radiation is gamma radiation.

Khaw et al. disclose a method of enhancing effects of therapy that kills diseased (malignant/tumor) cells in vivo by providing (immuno)liposomes specific for an internal cellular antigen present in degenerating neoplastic cells. Techniques are known for liposome targeting such as conjugating antibodies to cell-surface (malignant) antigens to pharmacologically active agents and labels to permit diagnosis, localization, and therapy toward tumors (see column 7, line 48 to column 8, line 3). The liposomes contain antineoplastic agent for initiating therapy in a mammal to kill malignant cells in vivo (see column 2, last paragraph). The antineoplastic agents include radiosensitizing agents, cytotoxic agents, and radionuclides (see column 3, first paragraph and column 4, lines 18-27). In diagnostic procedures, (immuno)liposomes containing radiosensitizer and diagnostic agent which are specific for intracellular antigens, such as an imaging agent, are injected into a patient receiving radiation therapy. Following administration, an imaging technique is employed using computed axial tomography (CAT) scan, X-ray imaging, including gamma ray imaging. (See column 16, line 18 to column 17, lines 3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer Rose Bengal taught by Serafini, Neckers, and Fondren using liposomal targeting technique as taught by Khaw because Khaw specifically taught that pharmaceutically of therapeutically activatable agents can be incorporated into liposomes or other delivery systems, for targeting delivery to specific tissue, ie. malignant tumors, which allows for localization of the agent into targeted specific tissues and Rose Bengal has been taught by Neckers to be

activatable by radiation. Further, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute use of gamma imaging as taught by Khaw into the teachings of Serafini, Neckers, and Fondren because use of gamma radiation is an obvious variation of imaging technique which is routinely known in the art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 22-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 6,331,286. Although the conflicting claims are not identical, they are not patentably distinct from each other because US Patent 6,331,286 discloses intracorporeal use of halogenated xanthene with ionizing radiation for treating diseased human tissue, i.e. cancer, by irradiating the halogenated xanthene that is administered into or proximate to the diseased human tissue.

Response to Arguments

15. Applicant's arguments filed 4/28/03 have been fully considered but they are not persuasive.

A) In responding to the rejection of the claims under 35 USC § 112, first paragraph (scope of enablement rejection), Applicant contends that the claims as currently recited, encompass an appropriate scope that is enabled by the specification, i.e a medicament ... for high energy phototherapeutic treatment ... of (any and all) human and animal tissue. Applicant argues that experimentation required to practice the claimed invention is normal within the field, i.e. establishing a required concentration and administration of the medicament via various conventional modes of delivery, is routine; thus appropriate guidance and examples have been provided. Applicant also argues that the claimed scope is enabled since other tissues and disease conditions are believed to be amenable to treatment via radiosensitization, using the claimed radiosensitizers.

Applicant's response is not persuasive because the claims are drawn to a medicament for incorporeal application into any human or animal tissue for use in high energy phototherapeutic treatment, regardless of type, i.e. normal tissue, and disease. However, both the specification and Applicant's response only provide that there is preferential accumulation of the halogenated xanthenes to diseased tissue such as tumors and have failed to take into account and prove or provide how this preferential or selective accumulation can be done on other tissue, absent the use of a targeting moiety incorporated into the halogenated

xanthene that selectively targets the diseased tissue so as to protect normal tissue, after the supposed administration of an appropriate dosage thereof.

In response to Applicant's argument that the claimed scope are intended to encompass those tissues and disease conditions that are believed to be amenable to treatment, via radiosensitization, using the claimed radiosensitizers stating that the therapeutic use of radiation for treatment of coronary disease is entirely possible, Applicant again has failed to prove or provide 1) that there is preferential accumulation of the halogenated xanthenes to diseased tissue encompassing coronary artery diseases, i.e. cardiac tissue, and 2) how the supposed administration of an appropriate dosage of halogenated xanthene can treat myocardial infarct, by exhibiting high intrinsic radiodensity to increase the therapeutic potential of ionizing radiation to the diseased tissue, knowing that desirable effects after treatment with the medicament and ionizing radiation, are reduction, elimination, or eradication of the diseased tissue, i.e. heart. As such, nowhere in the specification describes or exemplifies how a halogenated xanthene composition in combination with ionizing radiation can be used to treat any and all diseased tissue. Accordingly, Applicant's argument is not persuasive.

B) Applicant argues that Serafini only teaches diagnostic use of Rose Bengal and fails to teach any therapeutic use for Rose Bengal; thus, Serafini does not anticipate the claimed invention.

In response, the claimed invention recite 1) a medicament ... comprising halogenated xanthene as a primary active component, 2) use of halogenated

xanthene in the preparation of an intracorporeal medicament , 3) a pharmaceutical composition ... comprising halogenated xanthene, 4) an intracorporeally-applicable medicament comprising at least one halogenated xanthene as a primary component, 5) a pharmaceutical composition comprising a dosage unit of halogenated xanthene. Serafini teaches Rose Bengal, a halogenated xanthene as a pharmaceutical composition. Accordingly, Serafini et al. anticipates the claimed invention.

In response to applicant's argument that Serafini uses Rose Bengal for diagnostic purposes rather than therapeutic use, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Specifically, Applicant has not shown that the Rose Bengal known in the art and taught by Serafini is distinct from the Rose Bengal taught in the claimed invention.

C) Applicant argues that Serafini requires a special form of Rose Bengal, i.e. that contains radioactive isotopes of iodine whereas the radiosensitizer agents in the claimed invention are not radioactive. Applicant specifically argues

that the Rose Bengal used by Serafini is functionally different and has low toxicity in comparison to that used in the claimed invention.

In response, the claimed invention recite 1) a medicament ... comprising halogenated xanthene as a primary active component, 2) use of halogenated xanthene in the preparation of an intracorporeal medicament , 3) a pharmaceutical composition ... comprising halogenated xanthene, 4) an intracorporeally-applicable medicament comprising at least one halogenated xanthene as a primary component, 5) a pharmaceutical composition comprising a dosage unit of halogenated xanthene. Thus, use of comprising language does not exclude the teaching of Rose Bengal by Serafini. Further, the discovery of a new property of a known product, in this case, Rose Bengal, discovered to characteristically enhance efficacy of ionizing radiation in radiation therapy, does not render the product novel, unless otherwise, rendered novel or nonobvious from a modification or variation of its original structure, i.e. "ionized Rose Bengal" or "derivatized Rose Bengal", that is structurally different, novel, and nonobvious, from all other commercially known Rose Bengal.

D) Applicant reiterates that the present application is directed to halogenated xanthenes used as therapeutic medicaments, i.e. radiosensitizers, for use in enhancing the therapeutic efficacy of applied ionizing radiation. Applicant points throughout the specification on discussions of use of these halogenated xanthenes as radiosensitizing agents and reiterates that Serafini fails to teach such use.

In response to applicant's argument that Serafini fails to use Rose Bengal as radiosensitizing agents as recited in the claimed invention, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

E) Applicant argues that Neckers discloses none of the properties of any halogenated xanthene, i.e. radiosensitizer, relevant to its use with ionizing radiation.

In response, the claimed invention recite 1) a medicament ... comprising halogenated xanthene as a primary active component, 2) use of halogenated xanthene in the preparation of an intracorporeal medicament , 3) a pharmaceutical composition ... comprising halogenated xanthene, 4) an intracorporeally-applicable medicament comprising at least one halogenated xanthene as a primary component, 5) a pharmaceutical composition comprising a dosage unit of halogenated xanthene. Neckers teaches Rose Bengal, a halogenated xanthene as a composition. Accordingly, Neckers anticipates the claimed invention. Further, a discovery of a new property of a known product, in this case, Rose Bengal, discovered to characteristically enhance efficacy of

ionizing radiation in radiation therapy, does not render the product novel, unless otherwise, rendered novel or nonobvious from a modification or variation of its original structure, i.e. "ionized Rose Bengal" or "derivatized Rose Bengal", that is structurally different, novel, and nonobvious, from all other commercially known Rose Bengal.

In response to applicant's argument that Neckers fails to disclose therapeutic use of Rose Bengal, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Further, the discovery of a new property of Rose Bengal, discovered to characteristically enhance efficacy of ionizing radiation in radiation therapy, does not render the product novel, unless otherwise, rendered novel or nonobvious from a modification or variation of its original structure, i.e. "ionized Rose Bengal" or "derivatized Rose Bengal", that is structurally different, novel, and nonobvious, from all other commercially known Rose Bengal.

F) Applicant argues that the combination of Neckers with Norman does not render obvious the claimed invention because they both teach unrelated contrast media and have unrelated properties.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, Neckers teaches halogenated xanthene or Rose Bengal which is a known halogenated contrast or imaging medium. Norman, on the other hand, teaches gandolinium as a halogenated, i.e. iodinated, contrast medium. Norman was combined with the teaching of Neckers only for the use of irradiation at 140 keV to irradiate the halogenated contrast media. Thus, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to activate the halogenated xanthene of Neckers with ionizing radiation at 140 keV as used by Norman because gandolinium belongs to the same class of halogenated, i.e. iodinated, contrast medium, as the halogenated xanthenes taught by Neckers; thus, are obvious variations of iodinated contrast media known.

16. For reasons aforementioned, no claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is

(703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
September 9, 2003

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641